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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/016,969	12/14/2001	Richard A. Pittner	0401-UTL-0	7314

44638 7590 09/20/2004

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EXAMINER
LI, RUIXIANG

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 09/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/016,969	PITTNER ET AL.	
	Examiner	Art Unit	
	Ruixiang Li	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1,8 and 33-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,8 and 33-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *06/01/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, and/or Claims

The amendment filed on 07/15/2004 has been entered. Claim 45 has been amended.

Claims 1, 8, and 33-54 are pending and under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Information Disclosure Statement

The Information Disclosure Statement filed on 06/01/2004 has been considered by the Examiner and a fee of $180 as set forth in §1.17(p) has been charged to the Deposit Account No. 010535.

Withdrawn Rejections

The rejection of claims 45-47 under 35 U.S.C. §102 (b) as being anticipated by Okada et al., as set forth at pages 3-4 of the previous Office Action (Paper No. 02262004), has been withdrawn in view of Applicants' argument and amendment to the claims.

Claim Rejections Under 35 U. S. C. § 102 (b)

Claims 52-54 are rejected under 35 U.S.C. 102(b) as being anticipated by Morley et al (*Life Sci.* 41:2157-2165, 1987).

Morley et al. teach peripheral administration (subcutaneously) of peptide YY reduced body weight in 12-week-old mice (Abstract; Figure 5; section of methods). It is also noted that the property of PYY recited in claim 53 is inherent to the molecule of PYY. Thus, the reference of Morley et al. meets the limitations of claims 52-54.

Claim Rejections Under 35 U. S. C. § 102 (b)/103 (a)

(i) The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(ii) The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

(iii) This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

(iv) Claim 46 is rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Okada et al. (*The Endocrine Society 75th Annual Meeting Prograpm & Abstract*, page 180, Abstract 520B, 1993).

Okada et al. teach a method of reducing high fat diet intake comprising peripherally administering PYY to male Sprague-Dawley rats at the doses of 1, 10, 20, and 40 nmol (equivalent to about 4.3, 43, 86, and 172 μg, respectively; molecular weight of PYY=4310). Assuming the body weight of the rats are 200g, the doses of PYY taught by Okada et al. also fall reasonably within the dose range of PYY recited by the instant claims. Okada et al. further teach that PYY is a satiety factor for fat meal, meeting the limitations of claim 46.

Applicants argue that Okada et al. do not teach administration of PYY in the amount of 0.1 μg/kg to 10 μg/kg per day. This is not found to be persuasive because the claim recites "***about*** 0.1 μg/kg to 10 μg/kg per day" and thus the doses of PYY taught by Okada et al. fall reasonably within the dose range of PYY recited by the instant claim.

Claim Rejections Under 35 U. S. C. § 103 (a)

(i) Claims 45 is rejected under 35 U.S.C. 103(a) as being unpatentable over Okada et al. (*The Endocrine Society 75th Annual Meeting Programm & Abstract*, page 180, Abstract 520B, 1993).

Okada et al. teach a method of reducing high fat diet intake comprising peripherally administering PYY to male Sprague-Dawley rats at the doses of 1, 10, 20, and 40 nmol (equivalent to about 4.3, 43, 86, and 172 μg, respectively; molecular weight of PYY=4310). Assuming the body weight of the rats are 200g, the doses of PYY taught by

Okada et al. also fall reasonably within the dose range of PYY recited by the instant claims. Okada et al. further teach that PYY is a satiety factor for fat meal.

Okada et al. do not teach administering PYY to a human subject. However, it would have been obvious to one having ordinary skill in the art at the time the invention was made to administer PYY to a human subject to reduce appetite with a reasonable expectation of success in view of the teachings of Okada et al. on the rats. It is a logic step for one of skill in the art to develop a method of treating a human subject after a drug is tested successfully on an animal model.

(ii) The rejection of claims 1, 8, 33-44, 48-50, and 52-54 under 35 U.S.C. 103(a) as being unpatentable over Malaisse-Lagae et al. (*Experientia* 33:915-917, 1977) in view of Okada et al. (*The Endocrine Society 75th Annual Meeting Prograpm & Abstract*, page 180, Abstract 520B, 1993), Yoshinaga et al. (*Am. J. Physiol.* 263:G695-701, 1992), and Ueno et al. (*Gastroenterology*, 117:1427-1432, 1999), as as set forth at pages 4-6 of the previous Office Action (Paper No. 02262004, 03/03/2004), is maintained.

Claim 47 is also rejected on the same basis, as set forth at pages 4-6 of the previous Office Action (Paper No. 02262004, 03/03/2004).

From page 8 to page 13, Applicants, citing numerous references, argue that PYY and PP have very different binding profiles for receptors and biological functions. PP is expected to bind in a different tissue distribution pattern than PYY because of its

preference for the Y4 receptor. Applicants submit that while PP and PYY may share the function of inhibiting pancreatic exocrine secretion, the bulk of the literature would suggest to one of ordinary skill in the art that PP and PYY cannot be substituted for each other with a reasonable expectation of success. Applicants submit that it would not have been obvious to one of ordinary skill in the art to have substituted PYY for PP with a reasonable expectation of success.

Applicants' argument and the cited publications have been fully considered, but are not deemed to be persuasive for the following reasons. First, while PP and PYY have different binding profiles, as shown in the citing publications, the two peptides do share the following in common: both PP and PYY, when administered peripherally, decrease food intake, both belong to the pancreatic polypeptide family, and both function as an inhibitor of pancreatic exocrine, as taught by the cited art in the previous office action. It is these properties of the PYY polypeptide that motivates an artisan to substitute PP with PYY in the method of treating obesity known in the art.

Secondly, the present invention was obvious over the prior art at the time the invention was made. While there are various teachings ragarding the binding profies and activities of PYY and PP, the present invention is a logic evolution of the teachings of the prior art. As cited in the previous office action, Malaisse-Lagae et al. teach a method of treating obesity comprising administering to obese mice a therapeutive effective amount of pancreatic polypeptide. Peripherally administration of PP reduced food intake and

suppressed body weight. Okada et al. teach a method of reducing high fat diet intake comprising peripherally administering PYY to male Sprague-Dawley rats and that PYY is a satiety factor for fat meal. Yoshinaga et al. teach inhibition of pancreatic exocrine and gastric acid output by peptide YY and a PYY agonist, PYY3-36. Ueno et al. teach decreased food intake and body weight in pancreatic polypeptide-overexpressing mice and that physiological doses of PP inhibit pancreatic exocrine secretion. These teachings are clearly consistent with the concept that PYY can be used to reduce food intake and body wight. This position is supported by publications post the filing date of the instant application, including a publication in the journal of Nature (Batterham et al., Nature 418:650-654, August, 2002; submission date: January 9, 2002), which teaches that gut hormone PYY3-36 physiologically inhibits food intake and may be used for the treatment of obesity. Therefore, the present invention is pbvious over the teachings in the prior art. In orther words, it is obvious for one of ordinary skill in the art at the time the invention was made to use the PYY for treating obesity and reducing food intake with a reasonable expectation of success.

Moreover, Applicants' argument that Ueno used PP-overexpressing mice and did not exogenously administer PP is not persuasive because, as indicated in the previous office action, Ueno et al. teach physiological doses of PP inhibit pancreatic exocrine secretion (1st paragraph of right column of page 1427). In addition, it is known in the art that a transgenic animal is an effective tool for validating the biological functions of a molecule in animals.

At the bottom of page 13 of Applicants response, Applicants criticize the statement that one of ordinary skill in the art would understand that PYY could be substituted for PP because they both belong to the same PP/PYY/NPY family. Applicants submit that it is common for family members to have very different functions. This is not found to be persuasive because the previous office action states three factors, not just one regarding motivation: both PP and PYY decrease food intake, both belong to the pancreatic polypeptide family, and both function as an inhibitor of pancreatic exocrine, as taught by the cited art.

At the 2nd paragraph of page 15 of applicants' response, Applicants argue that while Malaisse-Lagae et al. describes PP as inhibiting food intake peripherally, PP was shown to be inactive in other study under similar copnditions. Applicants submit that half of the PP-overexpressing transgeni mice died in the study of Ueno, and no effect on body weight or adiposity was seen in Y4 receptor knockout mice. Accordingly, it was not clear from the litrature that PP had an effect food intake to a degree of significance.

Applicants' argument has been fully considered, but is not deemed to be persuasive for the following reasons. First, the study of Taylor et al shows PP at a dose of 200 nmol/kg was required to significantly reduce food intake in lean and obese mice; it does not show that PP is not active at all. Secondly, the study of Ueno et al. shows a decreased food intake and body weight in pancreatic polypeptide-overexpressing mice. As noted

by Ueno et al., PP overproduction led to postnatal lethality in half of the pups because of markedly decreased milk intake (see abstract). Thirdly, the fact that no effect on body weight or adiposity was seen in Y4 receptor knockout mice does not prove that PP has no effect on food intake and body weight because PP may cross react with other receptors, e.g., Y5. All things considered, one of ordinary skill in the art would reasonably believe that PP has an effect on food intake and weight reduction.

At the middle of page 15 of Applicants' response, Applicants argue submit that Okada et al. should not be credited with teaching more than it discloses. Examiner agrees. On the other hand, the teachings of Okada et al cannot be overlooked or minimized. Since Okada et al. teach a method of reducing high fat diet intake comprising peripherally administering PYY to male Sprague-Dawley rats and that PYY is a satiety factor for fat meal, the use of the reference of Okada et al in the office action is proper.

At the bottom of page 15 of Applicants' response, Applicants conclude that one of ordinary skill in the art could not have substituted PYY for PP with a reasonable expectation of success. This is not persuasive for the reasons above, as well as the reasons set forth in the previous office action.

At the bottom of page 15 of applicants' response, applicants noted that reducing foo intake is not necessarily linked to reduction of appetite. Applicants argue that food may be reduced for reasons unrelated to a reduction in appetite. For Example, in gastric

banding, appetite may remain unchanged while food intake is reduced. Also, a reduction in appetite may change the preference for certain foods that may or may not lead to a reduction in food intake. This is not persuasive because Applicants have not presented convicing evidence showing that reducing food intake is not linked to reduction of appetite in view of the instant disclsoure. The cited reference of Okada et al. teaches reducing high fat diet intake by PYY, which serves as a satiety factor for fat meal. A change in appetite from one type of food to another is not the same as a reduction in appetite for food.

Finally, at the 2nd paragraph of page 16, of Applicants response, Applicants argue that none of the cited references singly or combinded, suugest that PYY could be used to reduce weight, weight gain, or increase weight loss. This is not persuasive for the reasons above, as well as the reasons set forth in the previous office action.

(iii) The rejection of claim 51 under 35 U.S.C. 103(a) as being unpatentable over Malaisse-Lagae et al. in view of Okada et al., Yoshinaga et al., and Ueno et al., as applied to claims 1, 8, 33-44, 48-50, and 52-54, and further in view of Naslund et al. (Int. J. Obes. Relat. Metab. Disord. 23:304-311, 1999), as as set forth at pages 4-6 of the previous Office Action (Paper No. 02262004, 03/03/2004), is maintained.

Applicants argue that the reference of Naslund et al. does not cure the deficiencies of Malaisse-Lagae et al., Okada et al., Yoshinaga et al., and Ueno et al. as it does not teach, suggest or motivate one of ordinary skill in the art to substitute for PP in the

claimed method with a reasonably expectation of success. This is not persuasive for the reasons set forth above.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruixiang Li whose telephone number is (571) 272-0875. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, can be reached on (571) 272-0961.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [Brenda.Brumback@uspto.gov]. All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Ruixiang Li

Ruixiang Li, Ph.D.
Examiner
September 13, 2004